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TITLE: Vibratory Stimuli, A Novel Rehabilitation Method for Preventing Post – Traumatic Knee Osteoarthritis

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14. ABSTRACT

The purpose of this study is to determine and compare the acute effects of whole body vibration and local muscle vibration on quadriceps function, proprioception, and gait biomechanics in individuals with anterior cruciate ligament reconstruction. We hypothesize that both forms of vibration will equally enhance quadriceps function, proprioception, and gait biomechanics in manners that would potentially reduce the risk of developing knee osteoarthritis. While the specific aims will not be realized and cannot be analyzed until the study's completion in Year 3 due to the single-blind randomized controlled trial design, Year 1 of the project was highly successful regarding progress toward the study aims. The primary goal for Year 1 was to recruit and enroll the first cohort of 30 subjects. September 25, 2016 will mark the 1-year anniversary of HRPO approval and initiation of research activities in earnest. To date we have enrolled 19 subjects who have completed all testing and 1 who is currently participating, and are in the process of scheduling have scheduled 8 additional potential subjects for the initial screening session. These data are in agreement with the target enrollment rate of 6-8 subjects per quarter specified in the SOW. There have been no unanticipated problems, and data collection has proceed as planned.

15. SUBJECT TERMS
Knee, Osteoarthritis, Anterior Cruciate Ligament, Quadriceps, Inhibition, Muscle Dysfunction, Proprioception, Gait Biomechanics, Rehabilitation

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INTRODUCTION

Osteoarthritis (OA) is a leading cause of medical discharge from military service during both peacetime and armed conflict. Quadriceps dysfunction and proprioceptive deficits following traumatic knee injuries alter walking gait biomechanics in manners linked to development of knee OA. Current rehabilitation techniques are minimally effective for addressing these complications and preventing knee OA. Anterior cruciate ligament reconstruction (ACLR) dramatically increases the risk of knee OA, and represents an ideal model for evaluating novel rehabilitation techniques for preventing knee OA. Direct (local muscle vibration - LMV) and indirect (whole body vibration - WBV) vibratory stimuli enhance quadriceps function and proprioception, and may improve rehabilitation outcomes and reduce the risk of knee OA. The purpose of this study is to determine and compare the acute effects of WBV and LMV on quadriceps function, proprioception, and gait biomechanics in individuals with ACLR. We hypothesize that WBV and LMV will equally enhance quadriceps function, proprioception, and gait biomechanics in manners that would potentially reduce the risk of developing knee OA.

KEYWORDS

Knee, Osteoarthritis, Anterior Cruciate Ligament, Quadriceps, Inhibition, Muscle Dysfunction, Proprioception, Somatosensory, Gait Biomechanics, Rehabilitation

ACCOMPLISHMENTS

- **Major goals of the project for Year 1**
  - Attain research ethics approval
    - Local ethics approval was granted by the UNC-Chapel Hill Biomedical Institutional Review Board on 03-06-2015.
    - USAMRMC ORP HRPO ethics approval was granted on 25-09-2015.
  - Recruit and enroll the 1st cohort of 30 subjects
    - As of 31-08-2016, 20 of 54 identified potential subjects have been enrolled in the study
      - 18 subjects did not meet the inclusion criteria and were excluded
      - 7 subjects declined to participate
      - 1 subject enrolled but later dropped out
      - 19 subjects have completed their participation in the study (i.e. all 3 testing sessions)
      - 1 subject is currently engaged in data collection
      - 8 subjects are pending scheduling for the initial screening session

- **Accomplishments under goals**
  - The funding cycle for this project began on 01-08-2015. However, HRPO approval was not received until 25-09-2015. As such, the project was ongoing in earnest for only 10 months of the first year of funding. In that limited time period we have made substantial progress toward the goals of the project. As noted above, recruitment and enrollment of the 1st cohort of 30 subjects was to be completed in Year 1 per the SOW. As of 31-08-2016 we have enrolled 20 subjects of which 19 have completed their participation in the study and 1 is currently participating, and 8 subjects are currently pending scheduling for the initial screening session. Given the limited time allotted for enrollment during the first year (10 months) and the overlap with time intervals during which the university population from which we are primarily recruiting subjects is minimized

(e.g. winter break, summer break), this represents substantial progress toward the goals of the project.

- Data collection has progressed as planned with no adverse events or unanticipated problems. One subject screened into the study and reported to the laboratory for the first testing session, but withdrew during testing, stating "This reminds me too much of physical therapy and I don't want to continue." No adverse or unanticipated events occurred - the subject simply no longer wanted to participate.

- Analysis of the study aims is not possible at this time due to the single-blind randomized controlled trial design of the study. The aims will be evaluated following completion of data collection in Year 3.

- **Opportunities for training and professional development**
  - Nothing to Report

- **Dissemination**
  - Nothing to Report – the specific aims of the study will not be realized until its completion in Year 3 due to the single-blind randomized controlled trial design.

- **Plans for achieving goals in the next reporting period**
  - Recruit and enroll the 2nd cohort of 30 subjects
  - Continue with data collection as planned
  - Classes for the fall semester began at UNC-Chapel Hill on 23-08-2016. In only the first week of recruitment following the beginning of the fall semester we have identified 5 potential subjects, all of whom have either been enrolled or are pending scheduling for the initial screening session. We do not anticipate any difficulties in attaining these goals.

IMPACT

As per the SOW, all of the specific aims will be evaluated via the same randomized controlled experimental design that will conclude in Year 3 of the project. As such, the study's primary reportable outcomes will not be available until completion of the project.

- Development of the principal discipline
  - Nothing to Report
- Other disciplines
  - Nothing to Report
- Technology transfer
  - Nothing to Report
- Society beyond science and technology
  - Nothing to Report

CHANGES/PROBLEMS

Nothing to Report

PRODUCTS

Portions of the preliminary pre-intervention/baseline data were presented at the annual meetings of the Osteoarthritis Research Society International, Athletic Trainers' Osteoarthritis

Consortium, and National Athletic Trainers' Association. We anticipate that these preliminary data will lead to peer-reviewed journal publications with the addition of more subjects and increased statistical power in Year 2 of the project.

PARTICPANTS & OTHER COLLABORATING ORGANIZATIONS

The following individuals devoted at least one person month to the project:

Name	Troy Blackburn
Project Role	Principal Investigator
Nearest Person Month Worked	2
Contribution to Project	Dr. Blackburn has performed work related to the primary duties associated with the project including data reduction and analysis; software development for data reduction; subject recruitment; and supervision of RAs. He has also been responsible for the overall coordination of the project.

Name	Brian Pietrosimone
Project Role	Co-Investigator
Nearest Person Month Worked	1
Contribution to Project	Dr. Pietrosimone has played a vital role in oversight of the randomization process. He has also supervised the delivery of the interventions to preserve blinding for both the PI and RAs who are conducting data collection.

Name	Jonathan Goodwin
Project Role	Research Assistant
Nearest Person Month Worked	2
Contribution to Project	Mr. Goodwin has performed work related to subject recruitment; data collection and reduction; and calibration and maintenance of research equipment.

Name	Andrew Allen
Project Role	Research Assistant
Nearest Person Month Worked	1
Contribution to Project	Mr. Allen has performed work related to data collection and reduction.

Changes in active support

- Since the initial funding decision Drs. Blackburn and Pietrosimone have received additional funding and changes in active support via the following two grants:
    - Pietrosimone (PI) – *Improving disability in knee osteoarthritis by targeting neuromuscular deficits*

        - National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) – Pilot and Feasibility Clinical Research Grants Program (R21)
        - Funding Awarded: $418,000
            - This grant provides funding in the amount of 22% effort for Dr. Pietrosimone and 7% effort for Dr. Blackburn.

    - Pietrosimone (PI) – *Posttraumatic Osteoarthritis: Establishing a Comprehensive Evaluation Strategy*
        - National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) – Small Grant Program for New Investigators (R03)
        - Funding Awarded: $152,000
            - This grant provides funding in the amount of 11% effort for Dr. Pietrosimone and 0% effort for Dr. Blackburn.

These projects incur shared facilities with the current project, but involve different populations, thus they do not impact our ability to carry out the associated aims. The only notable influence on the current project is with respect to Dr. Pietrosimone's support. The university employs faculty on 9-month appointments, and limits the amount of additional income (e.g. via grants, contracts, summer school teaching, consulting, etc.) to 1/3 of the 9-month salary. For Year 1 of the project, the 33% summer funding detailed in the budget (i.e. 1 calendar month) would have exceeded Dr. Pietrosimone's total salary limit when combined with funding from the other sources. As such, this funding ($10,556) was not utilized for Year 1. No other changes occurred.

Involvement of Other Organizations

We have partnered with the Veterans Affairs Medical Center in nearby Durham, NC in an effort to recruit military veterans into the study as described in the original proposal. This partnership was made possible via collaboration with Dr. Kelli Allen who has a dual appointment at UNC-Chapel Hill and the Durham VA. We received final approval for recruitment from the VA on 17-11-2015, but did not gain approval to access medical records for identification of potential subjects until 14-06-2016. Unfortunately, this collaboration has not yet been successful due to the fact that only 47 potential subjects were identified (not included in the total of 53 referenced above), of which 22 did not meet all of the inclusion criteria and 17 were uninterested in participation primarily due to the requirement to travel large distances to the laboratory for multiple visits. Recruitment letters were sent to the remaining 8 potential subjects, of which 2 expressed further interest in participation. We are currently in the process of trying to schedule these individuals for the initial screening assessment.

Vibratory Stimuli: A Novel Rehabilitation Method for Preventing Post-Traumatic Knee Osteoarthritis

MR140103-Neuromusculoskeletal Injuries Research Award

Funding Opportunity Number: W81XWH-14-DMRDP-CRMRP-NMSIRA

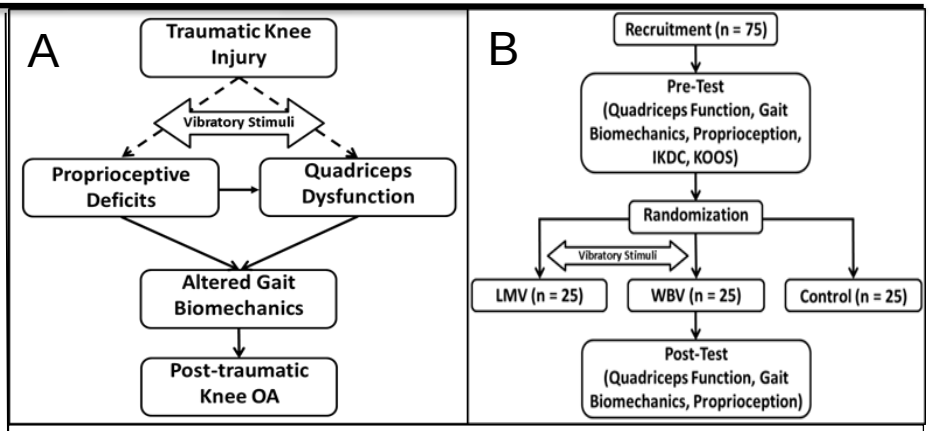
PI: Blackburn, J. Troy **Org:** University of North Carolina at Chapel Hill **Award Amount:** $772,058

Study/Product Aim(s)

- To determine the effects of whole body vibration (WBV) and local muscle vibration (LMV) on quadriceps function, proprioception, and gait biomechanics in individuals with anterior cruciate ligament reconstruction (ACLR)
- To compare the effects of WBV and LMV on quadriceps function, proprioception, and gait biomechanics in individuals with ACLR
- To identify factors that predict the effects of WBV and LMV on quadriceps function, proprioception, and gait biomechanics in individuals with ACLR

Approach

Individuals with ACLR within the past 5 years will be randomized to WBV, LMV, and Control groups (Figure B). Quadriceps function, proprioception, and gait biomechanics will be assessed prior to and following WBV and LMV interventions we demonstrated previously to improve quadriceps function, or a Control intervention.



A) Theoretical framework. Traumatic knee injuries (e.g. ACLR) result in proprioceptive deficits and quadriceps dysfunction which alter gait biomechanics in manners that contribute to post-traumatic knee osteoarthritis. We demonstrated that LMV and WBV improve quadriceps function, and WBV improves proprioception, thus these vibratory stimuli may also prevent alterations in gait biomechanics and reduce the risk of post-traumatic knee osteoarthritis. **B) Experimental design**

Timeline and Cost

Activities CY	16	17	18
Subject recruitment			
Data collection			
Data reduction and analysis			
Develop dissemination materials			
Estimated Budget ($K)	**$253**	**$258**	**$261**

Goals/Milestones

CY16 Goals

☐ Enroll initial cohort of 30 subjects

- 20 enrolled as of 31-08-2016

CY17 Goal

☐ Enroll second cohort of 30 subjects

CY18 Goal

☐ Enroll final cohort of 15 subjects

☐ Complete data collection, reduction, and analysis

☐ Develop dissemination materials